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73. Yoshio Sasaki, Miyoko Suzuki, Toshihiko Hibino, and Kazuko Karai : Studies on the Proton Magnetic Resonance Spectra in Aromatic Systems, I. Discussions on the Para-disubstituted-, 1-Substituted-3,4-Dimethoxy- and 1-Substituted-3,4-Methylenedioxy Benzene Derivatives.

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Proton magnetic resonance spectra of para-disubstituted benzene, 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series are investigated in the following items :

1. Ring proton chemical shift and shielding parameter.
2. Ring proton coupling constant and electronegativity of the substituent.
3. Inspection on the analysis of the spectra.
4. Side chain proton shift and Hammett's constant.

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It is often a troublesome task for organic chemist to analyse the ring proton magnetic resonance spectra in aromatic systems because of the unfavorable J/δ ratios. But, to resolve this difficulty, deuterium exchange by chemical method and spin decoupling are utilized, but they are not always effective.

However, for the estimation of the ring proton chemical shift in aromatic systems, the utilities of the so-called shielding parameters[1~3] are recently expected, which are the measures of the chemical shifts in the ortho, meta and para position caused by the substituents on the benzene nucleus.

In the present study, we have tried to estimate the reliability and the practical utility of a simple sum method of the shielding parameter, which had been previously suggested by P.L. Corio, *et al.*[4] and H.S. Gutowsky, *et al.*[5] in substituted benzene derivatives.

Hitherto, in aromatic systems many discussions have been established on the correlation of side chain proton shifts and Hammett's constants, but few clear-cut results have been obtained in the ring proton chemical shift and coupling constant owing to the co-operative effect of the ring current, the magnetic anisotropy of the substituent, etc.

In this papers, the proton magnetic resonance spectra of para-disubstituted benzene series, 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series were studied in the following items :

1. Ring proton chemical shifts and shielding parameters in the para-disubstituted benzene series, 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series.

2. Ring proton coupling constants and electronegativities of substituents in 1-substituted-3,4-dimethoxybenzene series.

3. Analyses of the spectra in 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series.

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1) H. Spiesecke, W.G. Schneider : J. Chem. Phys., **35**, 731 (1961).
2) J.S. Martin, B.P. Dailey : J. Chem. Phys., **37**, 1722 (1963).
3) P. Diehl : Helv. Chim. Acta, **44**, 829 (1961).
4) P.L. Corio, B.P. Dailey : J. Am. Chem. Soc., **78**, 3043 (1956).
5) H.S. Gutowsky, *et al.* : *Ibid.*, **74**, 4809 (1952).

4. Side chain proton chemical shifts in 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series.

Experimentals

Materials All samples were prepared by the authorized procedures.

Measurements of Spectra——1) All spectra were measured with a Hitachi Perkin-Elmer Model H-60 type spectrometer. The spectra were measured in dil. $CDCl_3$ solution (ca. 2.5×10^{-2} mol) and in dil. CH_2Cl_2 solution (ca. 0.5～1.0 mol), calibrated using Me_4Si as an internal reference. The resolution was checked by CH_3CHO quartets ($\lesssim 2.5\times10^{-9}$), and the accuracies of chemical shift and coupling constant were within 1.2 c.p.s. and 0.2 c.p.s., respectively.

2) Positive sign indicates a more shielding than that in C_6H_6, negative sign indicates a less shielding.

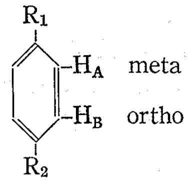
Results and Discussions

I. Ring Proton Chemical Shifts

1) Para-disubstituted Benzene Series

In 1962, J. S. Martin and B. P. Dailey[6] established the analyses of the ring proton chemical shift in numerous para-disubstituted benzene series.

Now we arranged their results in the derivatives of nitrobenzene, toluene, chlorobenzene, bromobenzene, aniline and benzene.



$R_1=NO_2$, Cl, Br, H, CH_3, NH_2
R_2=variable substituent

If the simple sum rule of the substitutent's shielding parameter holds in these series, the ring proton chemical shifts δ_{H_A}, and δ_{H_B} are as follows :

$$\delta_H\text{meta}=d_0\text{-}R_1+d_m\text{-}R_2$$

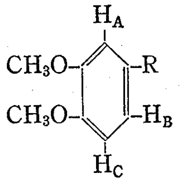
$$\delta_H\text{ortho}=d_0\text{-}R_2+d_m\text{-}R_1$$

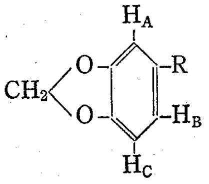
As is illustrated in Table I, the observed shifts[6] are compared with those of the calculated values from 3 parameters,[1~3] and among their data[6] linear $\delta_H$meta/δ_H ortho relations, which are also accepted from d_m-R/d_0-R ratio, of different gradient are obtained (cf. Fig. 1 and 2), and these correlations are shown as below (cf. Table II).

Accordingly, in these series the contribution from the perturbation provided by 2 substituents in para position affects a little on the ring proton shift, therefore, for the practical purpose, we are able to estimate the ring proton shift within ± 0.1 p.p.m.

2) 1-Substituted-3,4-dimethoxybenzene Series and 1-Substituted-3,4-methylenedioxy Benzene Series

In the above two series, whenever the substituent R is electron attracting or





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[6] J. S. Martin, B. P. Dailey : J. Chem. Phys., **37**, 2594 (1962).

TABLE I.

R_1	R_2	Observed		Calcd.[2]		Calcd.[3]		Calcd.[1]	
		H_A	H_B	H_A	H_B	H_A	H_B	H_A	H_B
NH_2	OCH_3	0.790	0.643	0.876	0.748	0.78	0.64	0.795	0.65
〃	Cl	0.808	0.275	0.735	0.271	0.74	0.15	0.78	0.18
〃	Br	0.877	0.130	0.902	0.112	0.79	0	0.838	−0.023
〃	I	0.968	−0.055	1.033	−0.092	0.90	−0.19	1.005	−0.20
〃	NO_2	0.677	−0.627	0.613	−0.684	0.47	−0.76	0.545	−0.75
〃	CH_3	0.823	0.418	0.875	0.454	0.81	0.39		
CH_3	〃	0.288		0.29		0.30			
〃	Cl	0.250	0.110	0.250	0.107	0.23	0.08		
〃	Br	0.305	−0.045	0.317	−0.052	0.28	−0.09		
〃	I	0.423	−0.257	0.448	−0.265	0.39	−0.28		
〃	NO_2	0.035	−0.825	0.028	−0.848	−0.04	−0.85		
Cl	Br	0.128	−0.092	0.134	−0.092	0.06	−0.16	+0.063	−0.198
Br	〃	−0.027		−0.125		−0.11		−0.14	
〃	I	0.108	−0.215	0.106	−0.229	0.00	−0.30	+0.027	−0.317
〃	NO_2	−0.330	−0.783	−0.314	−0.821	−0.43	−0.87	−0.433	−0.867
Cl	Cl	0.065		0.067		0.01		0.005	
〃	I	0.258	−0.286	0.265	−0.296	0.17	−0.35	0.23	−0.375
〃	NO_2	−0.160	−0.870	−0.155	−0.888	−0.26	−0.92	−0.23	−0.925
CN	Cl	−0.203	−0.103	−0.203	−0.100	−0.29	−0.18		
$COCH_3$	〃	−0.577	−0.092	−0.573	−0.091				
COCl	〃	−0.770	−0.157	−0.763	−0.156				
CHO	〃	−0.475	−0.177	−0.473	−0.195				
NO_2	NO_2	−1.147		−1.11		−1.19		−1.16	
CH_3	OCH_3	0.283	0.552	0.292	0.584	0.27	0.55		
OCH_3	Br	0.567	0.043	0.611	−0.051	0.53	−0.12	0.513	−0.183
〃	Cl	0.525	0.108	0.544	0.108	0.48	0.05	0.455	0.02
〃	NO_2	0.380	−0.887	0.322	−0.847	0.21	−0.88	0.22	−0.91

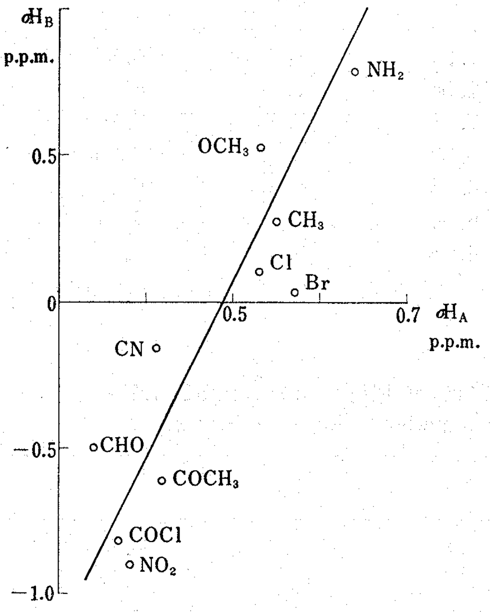


Fig. 1.

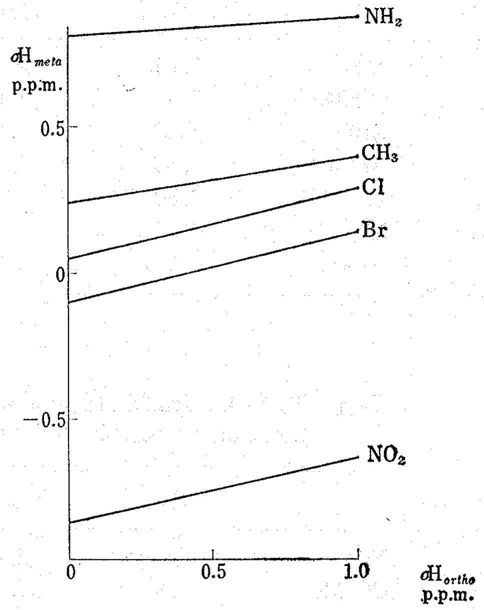


Fig. 2.

electron releasing, the ring proton chemical shifts are analysed by the first order rule (cf. Chart 1), but the other substituents make the splittings to coalesce into one broad signal.

Table Ⅱ.

Substituent R	Schielding Ratio $\delta_{H_{meta}}/\delta_{H_{ortho}}$	Substituent R	Schielding Ratio $\delta_{H_{meta}}/\delta_{H_{ortho}}$
NH_2	0.6/10	Cl	2.4/10
OCH_3	1.6/10	H	2.4/10
CH_3	1.5/10	NO_2	2.2/10
Br	2.4/10		

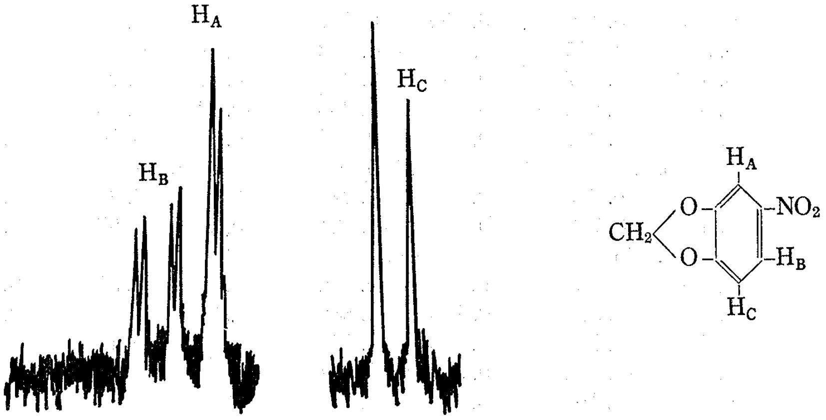


Chart 1.

In general, the ring proton shifts are in the following order, namely, $\delta H_B > \delta H_A > \delta H_C$, as is illustrated in Table Ⅲ and Ⅳ.

Table Ⅲ. Chemical Shifts (in p.p.m. from TMS) of Ring Proton and Coupling Constants (c.p.s.) in 1-Substituted-3,4-methylenedioxy Benzene Series

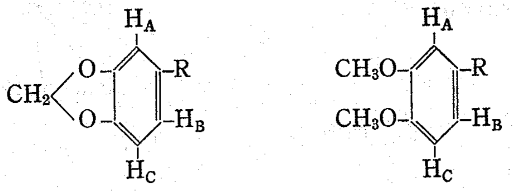
	A	J_{AB}	B	J_{BC}	C
NO_2	7.61	2.4	7.84	8.6	6.85
CO_2Me	7.40	1.6	7.56	7.9	6.79
CHO	7.27	1.6	7.38	7.9	6.90
Br	6.82		6.82		6.85
H	6.80		6.80		6.80
Me	6.64		6.64		6.64
NH_2	6.25	2.3	6.08	7.9	6.57

Table Ⅳ. Chemical Shift (in p.p.m. from TMS) of Ring Protons and Coupling Constants (c.p.s.) in 1-Substituted-3,4-dimethoxy Benzene Series

	A	J_{AB}	B	J_{BC}	C
NO_2	7.65	2.4	7.82	8.6	6.88
CO_2Me	7.53	1.8	7.66	8.2	6.86
CHO	7.38	1.7	7.40	8.2	6.95
Br	7.01	1.8	7.07	7.8	6.72
H	6.65	1.2	6.65	7.8	6.65
Me	6.74		6.74		6.74
NH_2	6.28	2.4	6.20	8.2	6.68

Hitherto, in polysubstituted benzene series, it has been suggested that ring proton chemical shift could be calculated by the simple sum method of the shielding parameter, and to confirm the above proposal, the calculated and observed shift in these 2 series has been examined. Shifts were calculated from H. Spiesecke and W.G. Schneider's[1] and J.S. Martin and B.P. Dailey's[2] parameters, which are proved favorable for the practical purpose (cf. Table V).

TABLE V. Comparison between the Observed and Calculated Shift



	Substituents	Observed[a]		Calculated	
				A	B
H_A	NO_2	−0.23	−0.27	−0.37	−0.47
	CHO	+0.11	0	+0.05	−0.10
	Br	+0.56	+0.37	+0.43	+0.25
	Me	+0.74	+0.64	+0.77	
	MeO		+0.84	+1.07	+0.90
	NH_2	+1.13	+1.10	+1.36	+1.23
H_B	NO_2	−0.46	−0.44	−0.43	−0.54
	CHO	0.00	−0.02	−0.02	−0.17
	Br	+0.56	+0.31	+0.36	+0.19
	Me	+0.74	+0.64	+0.70	
	MeO		+0.97	+1.00	+0.84
	NH_2	+1.30	+1.18	+1.29	+1.17
H_C	NO_2	+0.53	+0.50	+0.43	+0.27
	CHO	+0.48	+0.43	+0.39	+0.25
	Br	+0.53	+0.66	+0.72	+0.56
	Me	+0.74	+0.64	+0.70	
	MeO		+0.54	+0.70	+0.51
	NH_2	+0.81	+0.70	+0.86	+0.68

The shifts were calculated from A: J.S. Martin, B.P. Dailey's[2] and B: H. Spiesecke, W.G. Schneider's[1] parameters respectively.
a) Shifts are measured in p.p.m. relative to benzene (7.37 p.p.m.) in CH_2Cl_2.

In the dimethoxy benzene series the chemical shifts δ_{H_A}, δ_{H_B}, and δ_{H_C} are shown by the simple sum of the shielding parameter as follows:

$$\delta_{H_A}=d_o\text{-}R+d_o\text{-}OCH_3+d_m\text{-}OCH_3 \quad (1)$$

$$\delta_{H_B}=d_o\text{-}R+d_m\text{-}OCH_3+d_p\text{-}OCH_3 \quad (2)$$

$$\delta_{H_C}=d_m\text{-}R+d_o\text{-}OCH_3+d_m\text{-}OCH_3 \quad (3)$$

As is shown in the above section, there is disclosed a linear correlation between 2 parameters $d_o(R)/d_m(R)$. Consequently, from (1), (2) and (3) there must be established 3 linear relations among δ_{H_A}, δ_{H_B}, and δ_{H_C} (cf. Fig. 3,4).

And from the gradients of a set of 3 lines, it is assumed that in the electron releasing substitutent series H_A and H_B are 5~6 times more shielded than H_C and the relation is reversed in the electron attracting substituents series. This is an interesting evidence in contrast with the chemical reactivities in these two series, and

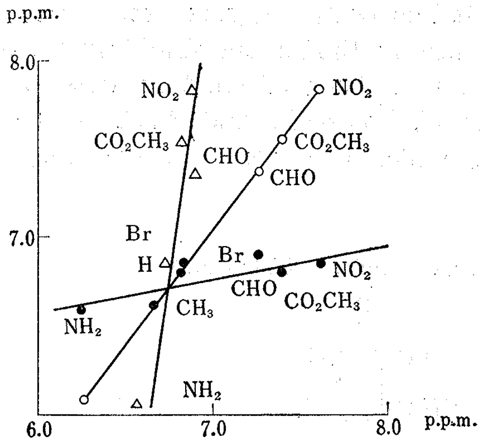


Fig. 3.

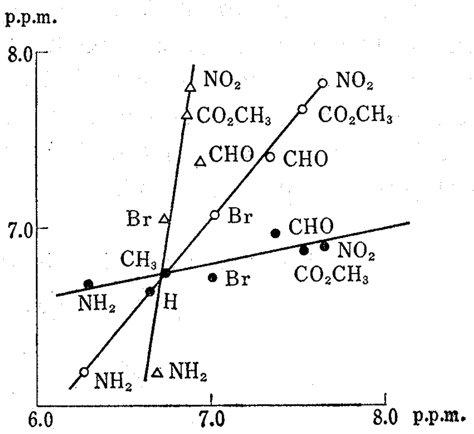


Fig. 4.

Correlations among δ_{H_A}, δ_{H_B}, and δ_{H_C} in 1-substituted-3,4-dimethoxybenzene series.
○ : $\delta_{H_B}/\delta_{H_A}$ △ : $\delta_{H_B}/\delta_{H_C}$ ● : $\delta_{H_C}/\delta_{H_A}$

an attempt is now being made to criticize the above results from the molecular orbital considerations.

Moreover, from the practical point of view, the shielding effect of the methylenedioxy group could be assumed approximately equal to that of dimethoxyl group, and considering the structural features in both system, it is concluded that the shielding effects of these groups are determined by 2 oxygen atoms attached to the benzene nucleus. Therefore, we can ignore the contribution from the alkyl residues. This results will be useful for the estimation of the ring proton chemical shift in the aromatic compounds with alkoxyl functions.

II. Coupling Constants in 1-Substituted-3,4-Dimethoxy Benzene Series

Several papers[1,2,7~9] are presented on the physicoorganic meaning of the coupling constant. As is shown in Fig. 5, there can be found linear relations between the coupling constants and the electronegativities of the atom attached to the ring carbon, then the observed ranges in the coupling constants are accord with the theoretical estimates

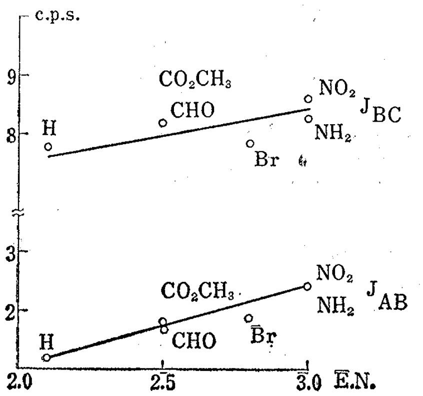


Fig. 5. Correlation between the Coupling Constants in 1-Substituted-3,4-dimethoxybenzene Series and Electronegativities.

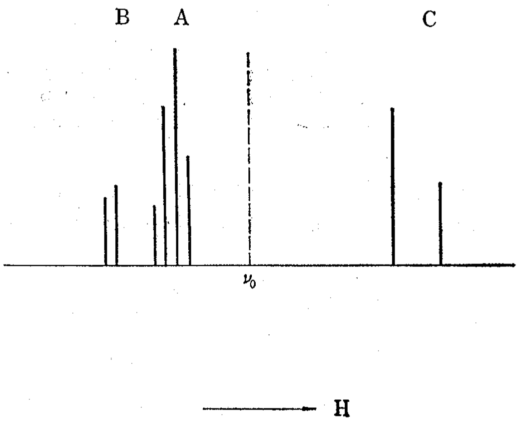


Fig. 6. Example 1-Methyl Veratrate

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7) H. M. McConnell: J. Mol. Spectry, **1**, 11 (1957), J. Chem. Phys., **30**, 126 (1959).
8) P. E. Cox: J. Am. Chem. Soc., **85**, 382 (1963).
9) M. Kondo: Bull. Chem. Soc. Jap., **38**, 1271 (1965).

proposed by H. M. McConnell[7] and others,[8,9] who suggest that these are dependent on the changes in moleculer orbitals, but the details of which will be discussed later.

III. Analyses of the Spectra

In this work, the analyses of the ring proton chemical shifts, and coupling constants in 1-substituted-3,4-dimethoxy and 1-substituted-3,4-methylenedioxy benzene derivatives are established.

In our case, the ring proton splitting belongs to the so-called ABC 3 spin system and the 6 spectral parameters-chemical shifts δ_{H_A}, δ_{H_B}, δ_{H_C} and coupling constant J_{AB}, J_{BC}, J_{CA}- are all variables. Moreover, the small chemical shift differences are unfavorable in the spin decoupling experiment, and in the deuterium exchange experiment the disappeared signal signifies not always the correct shift and coupling constant. Consequently, in the analysis of ABC 3 spin system, the spectral parameters are usually determined by an iterative method using a computer. Recently, T. Hirashima, *et al.*[10] established the practical inspection method of ABC 3 spin systen in the case of strong coupling from estimating the experimental "dispersion" Δ exptl. and calculated "dispersion" Δcal. Now we applied this method of analysis in the case of weak coupling and obtained favorable results.

1) Method of Inspection

Spectra were analysed in the case of weak coupling.

The details are as follows.

From the splitting patterns, ν_0 …… center of the spectral lines …… is estimated.

$$\nu_0=\nu_i/n$$

where $\nu_i=\nu_1$, ν_2, ν_3, ……, ν_{11}, ν_{12} …… chemical shifts of spectral lines.

n=number of spectral lines.

The 3 combination line, which are often unobservable on account of their weak intensities, must be found at $-2\nu_A$, $-2\nu_B$ and $-2\nu_C$[11] respectively.

Then from the experimental evidence, the experimental "dispersion" Δ exptl. is

$$\Delta\text{exptl.}=\frac{\{\Sigma\nu_i^2+4(\nu_A^2+\nu_B^2+\nu_C^2)-15\nu_0^2\}^{1/2}}{15}$$

On the other hand, ν_A, ν_B, ν_C, J_{AB}, J_{BC}, J_{CA} give the calculated "dispersion" Δcal. as follows :

$$\Delta\text{ cal.}=\frac{\{8(\nu_A^2+\nu_B^2+\nu_C^2)+3/16(J_{AB}+J_{BC}+J_{CA})^2+6(J_{AB}^2+J_{BC}^2+J_{CA}^2)\}^{1/2}}{15}$$

where ν_A, ν_B, ν_C indicate chemical shifts from ν_0, and J_{AB}, J_{BC}, J_{CA} indicate coupling constants.

For example the spectrum of methyl varatrate shows 12 lines, but 3 combination lines are estimated to be at $-2\nu_A$, $-2\nu_B$, $-2\nu_C$ as shown by asterisks.

	ν_i	c.p.s.		ν_i	c.p.s.		ν_i	c.p.s.
	ν_1	+31.4		ν_6	−9.3		ν_{11}	−12.7
ν_C	ν_2	+31.4	ν_A	ν_7	−9.3	ν_B	ν_{12}	−14.8

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[10] T. Hirashima, T. Kameo, O. Manabe, H. Hiyama : The Abstract Papers in the 19th Annual Meeting of the Chemical Society of Japan, Vol. **1**, 94 (1966) : Bull. Chem. Soc. Japan, in press.

[11] S. Castellano, J. S. Waugh : J. Chem. Phys., **34**, 295 (1961).

ν_3	$+23.3$	ν_8	-11.4	ν_{13}	-21.2
ν_4	$+23.3$	ν_9	-11.4	ν_{14}	-22.9
ν_5*	-54.7	ν_{10}*	$+20.7$	ν_{15}*	$+35.8$

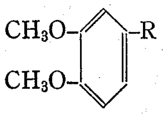
Δ exptl. $=6.53$ c.p.s.

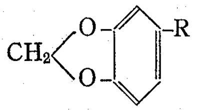
ν_C	$+27.4$ c.p.s.	J_{AB}	2.14 c.p.s.
ν_A	-10.4 c.p.s.	J_{BC}	8.15 c.p.s.
ν_B	-18.4 c.p.s.	J_{CA}	0. c.p.s.

Δ cal. $=6.54$ c.p.s.

The Δ exptl. and Δ cal. values in the 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series are summarized as follows: (cf. Table Ⅵ)

Table Ⅵ.





R	Δ exptl.	Δ cal.	Δ exptl.	Δ cal.
NO_2	8.21	8.24	8.26	8.30
CO_2Me	6.53	6.54	6.66	6.66
$COCH_3$	6.11	6.12		
CHO	4.20	4.25	4.12	4.08
Br	2.80	2.78		
NHAc	2.62	2.66		
OCH_3	3.70	3.79		
NH_2	4.38	4.38		
$CH{:}CH{\cdot}CO_2Me$			2.38	2.42

solvent: CH_2Cl_2

The Δ exptl. and Δ cal. values in the Table Ⅵ show a passable agreement. Unfortunately, when the ABC 3 spin system gives a nearly singlet structure -for example, 1-methyl-3,4-methylene-dioxy benzene-the above treatment is unsuccessful.

Moreover, as is stated in the above, Δ values depend mainly on the chemical shifts rather than the coupling constants in weak coupling cases. In spite of these limitations, this method of inspection has an interesting significance in the practical utility.

IV. Side Chain Proton Chemical Shifts in 1-Substituted-3,4-Dimethoxy-and 1-Substituted-3,4-Methylenedioxy Benzene Series

In the present papers, substituents R are all located on the para and meta position of the methylenedioxy and dimethoxy groups, therefore we have correlated the side chain proton shifts to σ_m, σ_p,[12] in the dimethoxy and to $\sigma_m+\sigma_p$ in the methylenedioxy series respectively, and obtained 2 liner relations of an equal gradient (cf. Fig. 7). Consequently, we are able to estimate as follows:

1. The both dimethoxy and methylenedioxy groups has a substituent effect of the same magnitude.
2. The two vic. OCH_3 groups has no steric interference.

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[12] R.W. Taft, Jr.: J. Phys. Chem., 64, 1805 (1960).

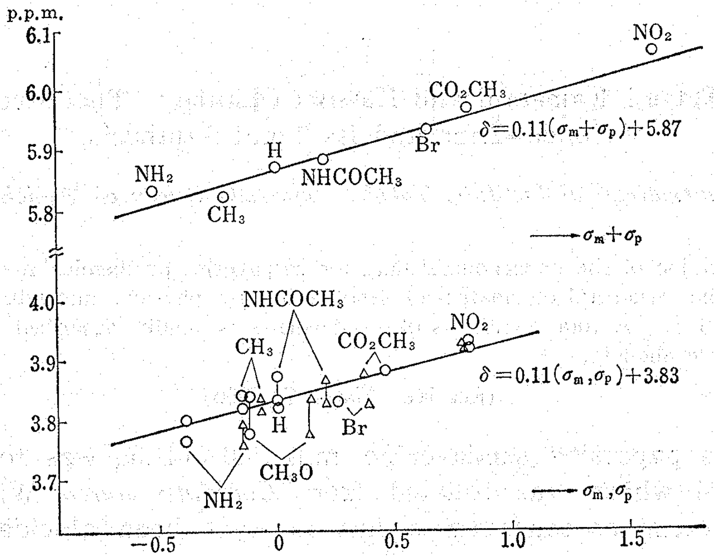

Fig. 7.

$\delta = 0.11(\sigma_m + \sigma_p) + 5.87$

Correlation between the side chain proton shift of 1-substituted-3,4-methylenedioxy benzene series and Hammett's constant.

$\delta = 0.11(\sigma_m, \sigma_p) + 3.83$

Correlation between the side chain proton shift of 1-substituted-3,4-dimethyoxy benzene series and Hammett's constant σ_m, σ_p.

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